

REMARKS

Claims 127 and 133 are pending in the instant application, once this amendment is entered. Claim 127 is amended to correct the typographical error as pointed out by the Examiner. Claim 127 has also been amended by incorporating the limitations previously recited by claim 129. Consequently, claim 129 is cancelled without prejudice. No new matter has been introduced.

A. The Rejection under 35 U.S.C. § 112, First Paragraph

In the Office Action, claims 127 and 133 are rejected under 35 U.S.C. § 112, first paragraph, allegedly for failing to comply with the written description requirement. In particular, it is alleged that the term “affective disorder,” as recited by claim 127, has “no clear description” in the specification (Office Action, page 3). Although Applicants disagree, especially in view of the fact that the term is well-known and understood by those skilled in the art, claim 127 is amended to recite specific affective disorders. In view of this amendment, Applicants respectfully request that the rejection be withdrawn.

B. The Rejection Under 35 U.S.C. § 103(a)

In the Office Action, claims 127 and 133 stand rejected as allegedly obvious over Morgan (US 6,274,579; 6,391,875; 2003/0064988) in view of Spier (*Depression and Anxiety*, 7:73-75 (1998)). In particular, it is alleged that “[t]he critical elements required by the claims are well taught” by Morgan, except the requisite secondary active compound. Morgan discloses (+)-(2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol ((S,S)-hydroxybupropion), which is alleged to be an active metabolite of bupropion. It is further alleged that “it would have been obvious to one of ordinary skill in the art at that time of the invention was made to add secondary active agent when Morgan is taken in view of Spier’s reference,” because Spier allegedly teaches a combination of bupropion with an SRI in the treatment of depression. Applicants respectfully traverse the rejection.

First, the method of combining bupropion with an SRI as described by Spier is distinctly different from the methods claimed in the instant application, which are

directed to a combination of an optically pure bupropion metabolite, (2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol, and an SRI for treating an affective disorder. As disclosed in Morgan, bupropion is metabolized *in vivo* into (+)- and (-)-hydroxybupropions, where the (-) form is the predominating metabolite (Col. 2, lines 16 to 20 in the '579 patent). As such, Spier's combination contains at least three chemical components *in vivo*, (+)- and (-)-hydroxybupropions, and an SRI, which is distinctly different from the two-component combination claimed in the instant application. Furthermore, it is unclear from Spier's report whether it is possible to simply eliminate the (-)-hydroxybupropion without any adverse effects on biological activity, metabolism, and toxicity profile of SRI.

Additionally, Morgan discloses that (S,S)-hydroxybupropion is about 10 fold less potent as a dopamine uptake inhibitor than bupropion (Col. 7, lines 26-28 in the '579 patent). It would have been counterintuitive to a person of ordinary skill in the art to replace bupropion in Spier's combination therapy with a much inferior dopamine uptake inhibitor, (S,S)-hydroxybupropion. This is especially true when Spier itself discloses that bupropion's "noradrenergic or dopaminergic effect" may attribute to the efficacy of its combination (Spier, page 25). In view of this disclosure, Morgan's finding that the claimed compound possesses much lower dopaminergic effect would have led those skilled in the art away from the claimed combination. As such, the presumption of obviousness established by the references cited by the Examiner, if any, would be rebutted in view of Morgan's teaching away alone.

Claims 127 and 133 also stand rejected as allegedly obvious over Howard (US 6,677,678) or Bertrand (EP 0701819) in view of Morgan (US 6,274,579). In particular, it is alleged that Howard discloses a method of combining an SSRI and a 5-HT agonist or antagonist for treating or preventing disorders arising from deficient or excessive serotonergic neurotransmission condition. Similarly, it is alleged that Bertrand discloses a method of combining an SSRI and a 5-HT agonist or antagonist for treating or preventing mood disorders. However, as the Examiner recognizes, Howard and Bertrand concern a combination of a serotonin reuptake inhibitor (*i.e.*, SSRI) and serotonin receptor agonist or antagonist (*i.e.*, 5-HT agonist or antagonist). Yet, as Morgan itself discloses, bupropion or the claimed metabolite, has nothing to do with serotonin reuptake (*See* Morgan, col. 7, lines 17, 18 and 21). Therefore,

Howard's and Bertrand's combination of two agents, the actions of both of which are through serotonin reuptake, cannot provide any suggestion whatsoever regarding a combination comprising the claimed compound, whose action does not concern serotonin reuptake. Consequently, Applicants respectfully submit that the rejection based on Morgan, Howard, and Bertrand should also be withdrawn.

C. The Double Patenting Rejection Should Be Withdrawn

Claims 127 and 133 stand provisionally rejected for nonstatutory obviousness-type double patenting over claims 13-15 and 58-78 of copending Application No. 09/987,930 in view of Spier, Howard, or Bertrand. Applicants respectfully request that the rejection be held in abeyance until allowable subject matter is indicated in the instant application and the '930 application, at which time Applicants will take appropriate action.

SUMMARY

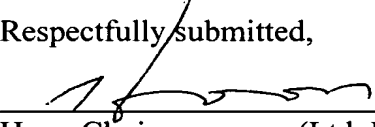
It is submitted that the foregoing amendment and remarks address all grounds of objection and rejection, and that the claims remaining in this application are in order for allowance.

Should the Examiner believe that prosecution of this application might be expedited by further discussion of any remaining issue, the Examiner is cordially invited to contact the undersigned representative of Applicants, Hoon Choi, by phone at (858) 314-1200.

Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 50-3013 and please credit any excess fees to such deposit account.

Date December 20, 2007

Respectfully submitted,


Hoon Choi
Jones Day

L0209
(Ltd. Recog. No.)

For: Anthony M. Insogna (Reg. No. 35,203)
Jones Day
12265 El Camino Real, Suite 200
San Diego, CA 92130
(858) 314-1200